DETAILED ACTION

1. Applicant's amendment, filed on August 26, 2011, is entered.

Claims 1-53, 75, and 81, 112 have been canceled.

Claims 54-74, 76-80, 82-111, and 113 are pending.

Claims 54-69, 73, 74, 76, 88-91, 94-105, and 107-111 stand withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on April 6, 2009.

Claims 70-72, 77-80, 82-87, 92, 93, 106, and 113 are currently under consideration as they read on the originally elected invention of non-blocking antibodies that bind FcγRIIb of SEQ ID NO:2.

2. In view of applicant's amendment, only following rejections have been set forth herein.

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claim 70 stands rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an antibody or antigen-binding fragment thereor, wherein the antibody specifically binds human FcγRIIb in the natural environment of the Fc receptor and does not interfere with immune complex binding to FcγRIIb, does not reasonably provide enablement for more.

Claims 77, 83, 84, and 87 stand rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an antibody or antigen-binding

fragment thereor, wherein the antibody specifically binds human FcγRIIb in the natural environment of the Fc receptor and does not interfere with immune complex binding to FcγRIIb, and wherein the antibody comprises the following structures:

A) a variable light chain having the amino acid sequence of SEQ ID NO:5,

B) a variable heavy chain having the amino acid sequence of SEQ ID NO:7,

C) a variable light chain having the amino acid sequence of SEQ ID NO:9,

D) a variable heavy chain having the amino acid sequence of SEQ ID NO:11,

E) a variable light chain having the amino acid sequence of SEQ ID NO:5 and a variable heavy chain having the amino acid sequence of SEQ ID NO:7 or SEQ ID NO:11,

F) a variable light chain having the amino acid sequence of SEQ ID NO:9 and a variable heavy chain having the amino acid sequence of SEQ ID NO:7 or SEQ ID NO:11, **OR,**

G) variable light chain CDRs1-3 from the variable light chains of SEQ ID NOs: 7 or 9 and variable heavy chain CDRs 1-3 from the variable heavy chains of SEQ ID NOs: 7 or 11 (must have all six CDRs of which three are from light chain and three from heavy chain).

does not reasonably provide enablement for more.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claim 70 is drawn to a substance that specifically binds to an artificial peptide or polypeptide comprising a conformationally discriminating epitope (CDE) in its native conformation, wherein the CDE is from SEQ ID NO:2 (representing FcγRIIb),

Claim 77 is drawn to an antibody or derivative thereof that activates the physiological function of human FcγRIIb or FcγRIIa.

Claims 83 and 84 are drawn to an antibody that is a polypeptide carrying a CDR or one or more CDRs which is specific for FcγRIIb.

Claim 87 is drawn to an antibody comprising the variable light or heavy regions of antibody according to SEQ ID NO:5 and 7, or a portion thereof having specificity, or the variable light or heavy regions of antibody according to SEQ ID NO:9 and 11 or a portion thereof having specificity.

Applicant's arguments have been fully considered but have not been found persuasive.

For initial matter, applicant asserts claim 77 has been withdrawn and thus the rejection does not apply to claim 77.

The examiner noted that the originally elected invention is drawn to a non-blocking antibodies that bind FcγRIIb of SEQ ID NO:2. Since claim 77 is drawn to an antibody that activates the physiological function of human FcγRIIb (similar to claim 113 that is currently under consideration), claim 77 is read as a non-blocking antibody that belongs to the originally elected invention rather than withdrawn invention.

Applicant argues the specification discloses procedures for producing antibody using routine methodologies. Applicant asserts that Examples 2 and 3 of the instant specification discloses detailed methods of immunizing mouse with antigen for antibody production and selection. Therefore, applicant asserts one of skill in the art would not need to carry out undue experimentation for the instant claims.

This is not found persuasive for following reasons:

The Examiner agrees with applicant that antibody production using immunization procedures of an antigen is routinely done by one of skill in the art. However, the problem here is that the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

While the specification discloses production and selection of antibody with the desired antigen specificity, the instant claims are drawn to a genus of:

a substance that specifically binds to an artificial peptide or polypeptide comprising a conformationally discriminating epitope (CDE) in its native conformation, wherein the CDE is from SEQ ID NO:2 (representing FcγRIIb) (in claim 70),

an antibody or derivative thereof that activates the physiological function of human FcγRIIb or FcγRIIa (in claim 77),

an antibody that is a polypeptide carrying a CDR or one or more CDRs which is specific for FcγRIIb (in claim 83 or 84), and

an antibody comprising the variable light or heavy regions of antibody according to SEQ ID NO:5 and 7, or a portion thereof having specificity, or the variable light or heavy regions of antibody according to SEQ ID NO:9 and 11 or a portion thereof having specificity (in claim 87).

There is insufficient objective evidence that antibodies specific for FcγRIIb, as disclosed in the specification as filed, can be extrapolated to predict the structure of a any or all substance, commensurate in scope with the claimed invention.

Further, as stated previously, it is well established in the art that the formation of an intact antigen-binding site generally requires the association of the complete heavy and light chain variable regions of a given antibody, each of which consists of three CDRs which provide the majority of the contact residues for the binding of the antibody to its target epitope. The amino acid sequences and conformations of each of the heavy and light chain CDRs are critical in maintaining the antigen binding specificity and affinity which is characteristic of the parent immunoglobulin. It is expected that all of the heavy and light chain CDRs in their proper order and in the context of framework sequences which maintain their required conformation, are required in order to produce a protein having antigen-binding function and that proper association of heavy and light chain variable regions is required in order to form functional antigen binding sites. Even minor changes in the amino acid sequences of the heavy and light variable regions, particularly in the CDRs, may dramatically affect antigen-binding function.

Furthermore, antibody having amino acid sequences that are highly homologous to the instant claims do not have the same function of "specifically blocking IgG binding to human FcγRIIb" as the instant claims. For example, as stated previously, Koenig et al. (US Patent 7,425,620, reference of record) teach a monoclonal antibody that specifically binds native human FcγRIIb which is endogenously expressed and present on surface of a cell with higher affinity than FcγRIIa (e.g. see column 9-16). Koenig et al. further teach a species of said antibody, 3H7, whose light chain variable region is 92.3% identical in amino acid sequence to the instant SEQ ID NO:5; the instant SEQ ID NO:5 shares at least the same CDR1 sequence to the prior art light chain variable region of 3H7 (see CDR1 location of the instant SEQ ID NO:5 on Figure 5 of the specification as-filed). As such, Koenig et al. also meet the limitations in claims 83, 84, and 97, encompassing "one

or more" CDRs from SEQ ID NO:5 and GB3 according to SEQ ID NOs: 5 and 7 or "a portion thereof having specificity", respectively. Yet, unlike the instant claims, Koenig's full length anti-FcγRIIb antibody blocks the binding of the immune complex binding to FcγRIIb (e.g. see columns 111-113).

As such, the specification provides insufficient direction or guidance regarding how to make and use the claimed substance or antibody as broadly defined by the claims other than ones described above. Undue experimentation would be required to produce the invention commensurate with the scope of the claims from the written disclosure alone.

In view of the quantity of experimentation necessary, the limited working example, the unpredictability of the art, the lack of sufficient guidance in the specification, and the breadth of the claims, it would take undue trials and errors to make the instant substance/antibody.

Therefore, applicant's arguments have not been found persuasive.

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
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> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

6. Claims 70-72, 77-80, 82, 83, 85, 86, 92, 93, 106, and 113 are rejected under 35 U.S.C. 102(e) as being anticipated by Koenig et al. (US Patent 7,425,620) as evidenced by the CDRs location of variable light region of mAbGB3 disclosed in Figure 5 of the instant specification and as further evidenced by Veri et al. (Immunology, 2007. 121:392-

404) regarding the non-blocking nature of the Fab fragment of 3H7 on right column on page 402 for the reasons of record.

Applicant's arguments, filed on August 26, 2011, have been fully considered but have not been found persuasive.

Applicant argues that the antibodies produced by clone 3H7 and 2B6 taught by Koenig et al. are both blocking antibodies that are different from the instant claims which are drawn to antibody that does not interfere with immune complex binding to FcγRIIb. Further, applicant asserts the evidentiary reference Veri et al. merely show that not all Fab fragments have the same activity and do not lead to blocking. Applicant argues Koenig et al. do not teach whether the anti-FcγRIIb antibodies bind the discriminating epitope (CDE) comprising amino acid 27 to 30 of the FcγRIIb region. Therefore, applicant asserts the prior art teachings do not anticipate the instant claims.

This is not found persuasive for following reasons:

Contrary to applicant's assertion that Koenig et al. do not teach blocking antibody, it is noted that the prior art teaches anti- FcγRIIb antibodies produced by deposited clones 2D11, 1D5, and 1F2, wherein the antibodies are able to distinguish the inhibitory FcγRIIb from activating FcγRIIa (e.g. see column 26 of Koenig et al.) and wherein the antibodies do not block immune complex binding to FcγRIIb (e.g. see evidentiary reference Veri et al. on right column on page 399 of Veri et al.).

Further, contrary to applicant's reliance on the binding to CDE epitope, it is noted that although Koenig et al. is silent about the antibodies binding to CDE epitope, it does not mean that the reference antibodies do not have this property. Since the office does not have a laboratory to test the reference antibodies, it is applicant's burden to show that the reference antibodies do not bind CDE epitope including epitope of comprising amino acids 27 to 30 of the FcγRIIb as recited in the claims. See *In re Best,* 195 USPQ 430, 433

(CCPA 1977); *In re Marosi*, 218 USPQ 289, 292-293 (Fed. Cir. 1983); *In re Fitzgerald* et al., 205 USPQ 594 (CCPA 1980).

As such, applicant's arguments have not been found persuasive.

7. No claim is allowed.

8. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chun Dahle whose telephone number is 571-272-8142. The examiner can normally be reached on 8:30-5:00. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisors Ram Shukla or Phuong N. Huynh can be reached 571-272-0735 and 571-272-0846, respectively. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Chun Dahle/
Primary Examiner, Art Unit 1644